

Epitomes

Important Advances in Clinical Medicine

Preventive Medicine and Public Health

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The Council on Scientific Affairs of the California Medical Association presents the following epitomes of progress in preventive medicine and public health. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and clinical importance. The items are presented in simple epitome, and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist busy practitioners, students, researchers, and scholars to stay abreast of progress in medicine, whether in their own field of special interest or another.

The epitomes included here were selected by the Advisory Panel to the Section on Preventive Medicine and Public Health of the California Medical Association, and the summaries were prepared under the direction of Dr Thom and the Scientific Advisory Panel to the Section on Preventive Medicine and Public Health.

***Escherichia coli* O157:H7 Infections**

ALTHOUGH *Escherichia coli* is a normally benign intestinal bacterium, certain strains cause diarrhea through several pathogenic mechanisms. In 1982 a restaurant-associated outbreak of bloody diarrhea resulted in the recognition of *E coli* O157:H7, the most common enterohemorrhagic serotype.

Escherichia coli O157:H7 causes diarrhea that is sometimes bloody and is often accompanied by severe abdominal cramps, vomiting, nausea, or a slight fever. In around 5% of persons with *E coli* infections, the hemolytic uremic syndrome develops, characterized by hemolytic anemia, thrombocytopenia, and temporary or permanent renal impairment. Asymptomatic infection is rare, but has been documented during outbreaks. Other complications are thrombotic thrombocytopenic purpura, unnecessary surgical intervention, coma or seizures, pancreatitis, and diabetes mellitus. A small percentage of symptomatic *E coli* O157:H7 infections are fatal.

The differential diagnosis of bloody diarrhea includes infections with *Shigella* species, *Campylobacter jejuni*, and *E coli* O157:H7. Because *E coli* O157:H7 requires special media and is not identified on routine stool culture, nonbloody diarrhea caused by the organism may go unrecognized. When a health maintenance organization in the Puget Sound area of Washington State screened all diarrheal stool specimens, *E coli* O157:H7 was identified as commonly as *Shigella* species, suggesting the organism is underdetected. Cultures for *E coli* O157:H7 may be negative if the stool specimen is obtained late in the course of the infection.

Beef, particularly incompletely cooked ground beef, is the most commonly reported food exposure in cases of *E coli* O157:H7 infection. Other foods associated with out-

breaks include raw milk and items presumably cross-contaminated with raw beef. One outbreak was caused by cider made from apples collected from the ground in an orchard where cows roamed. Outbreaks have also been associated with contaminated drinking or swimming water. Secondary transmission has been found within families and in day-care centers. No outbreaks have been attributed to ill food handlers.

Although *E coli* O157:H7 infection is not reportable in most states, it has been reportable in Washington State since 1987. Each year in Washington there are about 300 sporadic cases of *E coli* O157:H7 infection, primarily the result of mishandling meat items at home. During the first two months of 1993, the state had a large *E coli* O157:H7 outbreak associated with a fast-food chain. There were 477 people with positive cultures or the hemolytic-uremic syndrome, including 52 (11%) secondary cases. Of the 477 patients, 144 were admitted to hospitals, the hemolytic-uremic syndrome developed in 30, and 3 died. Hamburger meat from the chain grew the outbreak strain.

Antimotility agents should not be given to a patient with *E coli* O157:H7 infection. Antibiotic treatment does not appear to affect the disease course. Some studies suggest a poorer outcome with the use of trimethoprim and sulfamethoxazole or gentamicin sulfate. Hydration should be maintained initially and the patient observed for evidence of anemia, thrombocytopenia, or acute renal impairment. The hemolytic uremic syndrome may develop within a week of the initial diarrheal symptoms, in which case fluid and electrolyte management is necessary, including prompt dialysis if anuria or oliguria develops.

Cooking meat completely and avoiding cross-contamination with raw meat will reduce the risk of infection with *E coli* O157:H7. When a case occurs in a family, strict sanitation is important. Exclusion from day care un-

til the infection is cleared was recommended during the Washington outbreak. As other states add infection with *E coli* O157:H7 to reportable disease lists, it will likely be reported in most of the country.

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Controversy in Clinical Cancer Screening—Mammography

MAMMOGRAPHIC SCREENING to detect curable breast cancer has become one of the most widely recommended and accepted procedures in clinical preventive medicine. Although its benefit is well established for women between the ages of 50 and 69, its routine use with younger women, increasingly common in the past decade, has recently been challenged by new data and by expert review.

Eight major randomized clinical trials have now been reported. None has shown survival benefit at five to seven years' follow-up for women screened at ages 40 to 49, and meta-analysis of combined results shows a nearly equal risk of breast cancer death among those screened and those not screened. One early trial suggests a lower mortality at 10 to 18 years' follow-up in the mammography group, but its statistics are disputed. There is methodologic controversy about each of the studies, but the cumulative weight of the evidence has led the National Cancer Institute to withdraw its previous recommendation for the routine screening of women aged 40 to 49 years. Monthly self-examination and yearly examination by a physician are still considered prudent for all women older than 40. The American Cancer Society has not changed its advisory that all women older than 40 be offered mammography.

Mammography tends to be less accurate in younger women. The lower breast fat content before menopause makes the breast less radiolucent and mammography less sensitive, with more chance of missing cancers and giving falsely negative results. Conversely, greater breast density before menopause increases the risk of misinterpreting local densities as possible neoplasms, making mammography less specific, with more falsely positive results. Lower sensitivity and specificity, combined with a lower prevalence of cancer, make it less likely that an abnormal mammogram in a younger woman will actually prove to be cancer. This lower predictive value of a positive test is the screening statistic of particular interest to clinicians who must advise the next step in evaluating a positive screening test. A recent report of a large screening program in the San Francisco Bay Area is instructive. Abnormalities seen on mammograms (requiring evaluation for possible cancer) among 40- to 49-year-olds had

only a 1-in-25 chance of turning out to be cancer (a positive predictive value of 4%). The positive predictive value increased twofold in women aged 50 to 59 and fourfold in women aged 60 to 69. Women 40 to 49 years old with a family history of breast cancer had a positive predictive value (13%) three times that of others.

A history of breast cancer in a mother or sister at an early age provides the best current marker for an increased risk of cancer before age 50. A study of one large cohort found such women to be at a fivefold greater risk of fatal breast cancer. Genetic tests for this factor are being developed. Meanwhile, the growing reluctance to recommend routine mammographic screening of younger women should not deter its inclusion in clinical surveillance when family history indicates high risk.

Data are sparse for assessing the value of screening the increasing proportion of healthy women who are older than 70. The positive predictive value of mammography at this age, however, exceeds that of all younger age groups. The underrepresentation of older women in clinical trials should not exclude them from the benefits of early detection when clinically indicated.

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Controversy in Clinical Cancer Screening—Prostate-Specific Antigen

AS THE POPULATION has aged, prostate cancer has become the most commonly diagnosed cancer in men and the second most common cause of cancer deaths in men. That cancer confined to the prostate gland can be cured by radiation or surgical therapy provides strong incentive for early detection and perhaps screening. This is countered by the cancer's often indolent pattern of growth and metastasis and the morbidity associated with costly treatments. Thus, screening benefit decreases with age. The lifetime risk of prostate cancer developing in a 50-year-old man is estimated—from autopsy reports of its high prevalence in the elderly—as 42%, with only a 9.5% risk of clinical disease and a 2.9% risk of dying of prostate cancer. There are no data on the morbidity and mortality benefits of screening for prostate cancer comparable to those supporting routine mammography for breast cancer among women aged 50 to 70. A large trial is being developed, but results are 10 to 20 years away.

Assay of the prostate-specific antigen (PSA) has been increasingly advocated for detecting curable cancer, with a serum level greater than 4 µg per liter (4 ng per ml) generally taken as requiring further evaluation. The best estimates on PSA efficacy in the general screening of 50-